Reprogramming Differentiated Human Cells to a Pluripotent State

Grant Award Details

Reprogramming Differentiated Human Cells to a Pluripotent State

Grant Type: SEED Grant

Grant Number: RS1-00319

Investigator:

Name:	Thomas Wandless
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: iPS Cell

Award Value: $380,005

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Reprogramming Differentiated Human Cells to a Pluripotent State

Public Abstract:

If the therapeutic potential of human embryonic stem (ES) cells is to be realized, the ability to produce pluripotent stem cells with defined genetic backgrounds is essential. Pluripotent cells, through differentiation, have the ability to become any cell type. For basic and applied research, access to human ES cells derived from patients with specific diseases would be very valuable. In a more therapeutic setting, the ability to isolate differentiated cells from an individual patient and reprogram these cells to a pluripotent, stem-like state may ultimately lead to truly personalized medicine. Thus, an understanding of the genes that establish and maintain the pluripotent state of human ES cells is critical to future medical applications.

The overall goal of this research program is to establish an experimental protocol to efficiently reprogram differentiated human cells into a pluripotent state. It has recently been shown that the expression of only four genes in mouse fibroblasts reprograms these cells to a pluripotent state. We will pursue a similar strategy using differentiated human cells. Importantly, we have recently developed a new technology for regulating protein expression in human cells, and this technology will allow us to regulate the expression levels of these reprogramming proteins with unprecedented control.

The first half of this proposal focuses on the regulated expression of several genes that are known to be involved in the establishment and maintenance of pluripotency in human ES cells. By using our technology to regulate the levels of these proteins in differentiated cells, we will define the expression levels that lead to efficient nuclear reprogramming. The second half of this proposal will focus on epigenetic reprogramming. Epigenetic marks are modifications to DNA and the supporting histones that do not change the actual DNA sequence but that regulate gene expression. We will use our new technology to regulate the expression of proteins that are involved in maintaining the epigenetic state that is characteristic of embryonic stem cells. We believe that expression of these epigenetic modifiers, coupled with the regulated expression of pluripotency-inducing genes, will dramatically improve the efficiency for reprogramming differentiated cells to a pluripotent state.

Statement of Benefit to California:

Pluripotent cells such as embryonic stem cells, through the processes of differentiation, have the ability to become any cell type. If the therapeutic potential of human embryonic stem cells is ever to be realized, the ability to produce pluripotent stem cells with defined genetic backgrounds is essential. Access to human ES cells derived from patients with specific diseases would be very valuable for both basic and applied research. In a more therapeutic setting, the ability to isolate differentiated cells from an individual patient and reprogram these cells to a pluripotent state may ultimately lead to novel treatments for human diseases. Thus, an understanding of the genes that establish and maintain the pluripotent state of human ES cells is critical to future medical applications.

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